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***Review** / Derleme*

Building a patient blood management program in a large-volume tertiary hospital setting: Problems and solutions

Büyük ölçekli hastane düzeninde hasta kan yönetimi programının oluşturulması: Sorunlar ve çözümleri

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ABSTRACT

Successful implementation of a patient blood management program necessitates the collaboration of a strong organization and a multidisciplinary approach. We organized a meeting with broad participation in our center to establish a consensus for implementation of a specific patient blood management program. International and domestic experiences were shared, the importance of coordination and execution of different pillars in patient blood management were discussed, and the problems about the blood transfusion system were also investigated with the proposal for solutions. The data obtained from this meeting are presented to be a guide for similar large-volume tertiary hospitals for integration of a patient blood management protocol.

Keywords: Anemia-iron deficiency; blood preservation; blood transfusion; hemorrhage.

ÖZ

Hasta kan yönetimi programının başarılı bir şekilde uygulanması, güçlü bir organizasyon iş birliği ve multidisipliner bir yaklaşım gerektirir. Merkezimizde spesifik bir hasta kan yönetimi programının uygulanmasına yönelik bir konsensüs oluşturmak amacıyla geniş katılımlı bir toplantı düzenlendi. Uluslararası ve yerel deneyimler paylaşıldı, hasta kan yönetiminde farklı ayakların koordinasyonu ve yürütülmesinin önemi tartışıldı ve kan nakli sistemine ilişkin sorunlar çözüm önerileri ile birlikte ele alındı. Bu toplantıdan elde edilen veriler, hasta kan yönetim protokolü entegrasyonu açısından benzer büyük ölçekli üçüncü basamak hastaneler için de rehber olabilmesi amacıyla paylaşıldı.

Anahtar sözcükler: Anemi-demir eksikliği; kan koruma; kan nakli; kanama.

The World Health Organization (WHO) described the patient blood management (PBM) in the early 2000s, which was made effective in the Netherlands for the first time. In 2008, Australia was the first country which made it compulsory nationwide.[1-3] The United States, in 2007, published a guideline on bleeding and blood management before and after cardiac surgery.[4] The criticism and suggestions were considered for four years and were used to reform the guideline in 2011.[5] The European PBM guideline was published in 2017,[6] and the Turkish guideline was published in 2019.[7] Numerous studies conducted in these countries endorsed 30 to 40% reduction in the number of blood transfusions, significant resource

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savings, and a significant reduction in morbidity and mortality of patients.

The PBM is a three-pillar strategy to cure preoperative anemia and iron deficiency (intravenous [IV] iron + erythropoietin [EPO] + vitamin B12 + folic acid), reduce preoperative red blood cell (RBC) loss by an improved surgical technique, cell salvage, and re-transfusion, acute normovolemic hemodilution, coagulopathy management (anti-fibrinolytics, fibrinogen, Factor XIII, prothrombin complex concentrate [PCC], low central venous pressure, no hypertension, normothermia), and optimize anemia management (tolerate low hemoglobin values, IV iron + EPO postoperatively, increased fraction of inspired oxygen [FiO_2]).[8-13]

In this review, we aimed to share previous experiences and indicate current problems with solutions which would ensure the implementation of a PBM protocol in our hospital that can be also a guide for similar large-volume tertiary hospitals.

SUCCESSFUL IMPLEMENTATION STORIES: INTERNATIONAL

University Hospital of Zurich PBM Program

The University Hospital of Zurich (USZ) aimed to achieve the best possible surgical patient outcome (lowest mortality, no organ dysfunction, no lung injury, no renal impairment, no stroke, no myocardial infarction, minimal infection rate, minimal thromboembolic adverse events, minimal length of hospital stay, least amount of blood product transfusions, minimal costs) and adopted the strategies of PBM to attain this target.

Key steps in the implementation of PBM included the development of hospital-wide guidelines, creating a commission for the responsible use of blood products, achieving general ownership at all disciplines, monitoring guideline adherence, and collecting data to evaluate the success rate. Firstly, the anesthesiology department, in collaboration with the hematology department, developed evidence-based transfusion and anemia management guidelines (Tables 1 and 2). Eight specialties were defined to use these guidelines: cardiac surgery, trauma, transplantation, obstetrics, neurosurgery, burn unit, intensive care unit (ICU), and plastic surgery. Patients with an RBC transfusion rate of >10% and an expected blood loss of >500 mL were included as the focus group identified by the workgroup of USZ. The PBM program organization is listed in Table 3.

The PBM was put into practice in USZ about 10 years ago, and its success was demonstrated in many studies.[14,15]

SUCCESSFUL IMPLEMENTATION STORIES: NATIONAL

Numune Training and Research Hospital

The cardiovascular surgery clinic of Ankara Numune Training and Research Hospital in 2016 was one of the pioneers in launching the first applications of PBM in Turkey (Table 4). Thus, a two-step project was implemented: firstly, initiating a PBM program in the cardiovascular surgery clinic and subsequently, spreading out the program to the entire hospital after accomplishing successful outcomes.

Table 1. University Hospital of Zurich Guideline-Hemoglobin thresholds for transfusion

Healthy parturient	Hb <60 g/L
Patients without significant comorbidities	Hb <70 g/L
Patients with • SaO_2 <90% despite optimized ventilation • Severe traumatic brain injury • Free flaps • Severe (>70%) carotid stenosis	Hb <80 g/L
Patients with unstable coronary artery disease	Hb <90 g/L
No indication	Hb ≥90 g/L
Surgery stopped → evaluation	Hb <100 g/L unexpectedly
Pre-treatment according to Table 2	Hb 100-129 g/L or iron deficiency at Hb ≥130 g/L
Patients of the focus group can be operated if →	Hb ≥130 g/L men and women and no iron deficiency (Ferritin ≥100 μg/L and TSAT ≥20%)

SaO2: Oxygen saturation; Hb: Hemoglobin; TSAT: Transferrin saturation.

Table 2. University Hospital of Zurich Guideline-Preoperative treatment of anemia

Hemoglobin	Iron parameters Kidney function (Low grade) infection	Treatment
Hemoglobin <130 g/L "ID Anemia"*	Ferritin <100 µg/L or TSAT <20% CCL ≥50 mL/min	20 mg/kg BW iron carboxymaltose (IV) 30 min + 1 mg vitamin B12 (sc) + 5 mg folic acid (po)
Hemoglobin <130 g/L "Renal anemia"	Ferritin ≥100 µg/L and TSAT ≥20% CCL <50 mL/min	Epoetin alpha 600 U/kg BW 20 mg/kg BW iron carboxymaltose (IV) 30 min + 1 mg vitamin B12 (sc) + 5 mg folic acid (po)
Hemoglobin <130 g/L "Anemia of chronic disease"	Ferritin ≥100 µg/L and TSAT ≥20% CRP >5 mg/L	Epoetin alpha 600 U/kg BW 20 mg/kg BW iron carboxymaltose (IV) 30 min + 1 mg vitamin B12 (sc) + 5 mg folic acid (po)
Hemoglobin ≥130 g/L "Isolated ID"	Ferritin <100 µg/L or TSAT <20%	20 mg/kg BW iron carboxymaltose (IV) 30 min

*Surgery in <5 days → additionally Epoetin alpha 600 U/kg BW; TSAT: Transferrin saturation; CCL: Creatinine clearance; IV: Intravenous; po: Per oral; sc: Subcutaneous; BW: Body weight; CRP: C-reactive protein; ID: Iron deficiency.

Staff training, transfusion monitoring, IV fluid restriction, preoperative anemia treatment (IV iron carboxymaltose), revision and adaptation of international guidelines, and cooperation with cardiology were the parts of the preoperative phase.[16] The preoperative phase included goal-directed coagulation (impaired platelet function, surgical bleeding, etc.), goal-directed perfusion (low blood pressure or anemia may not be indicative of blood transfusion every time, what is important is the oxygen that penetrates the tissues), minimally invasive surgery, routine tranexamic acid administration, cerebral/somatic oximetry, minimally invasive extracorporeal circulation circuits, microplegia, retrograde autologous priming, vacuum-assisted venous drainage, ultrafiltration, cytokine adsorption, and recirculation of waste blood. The postoperative phase comprised of transfusion monitoring, IV fluid restriction, fibrinogen concentrate administration, and goal-directed coagulation tests.

A remarkable reduction in the use of blood and blood products after this PBM program was evident in the cardiovascular surgery clinic (Figure 1). A significant cost reduction was also achieved by implementing the PBM program. To accurately determine the cost of blood in this population, the activity-based costing (ABC) model was used as described by Shander et al.[17] The cost of approximately 42 triple coronary artery bypass surgeries was saved. Hospital records documented early extubation of patients accompanied by reduction of bleeding rates, shortening of the length of stay in hospital and ICU, and reduced mortality rate. Therefore, PBM was also successful in improving clinical outcomes. In the light of these data, Numune Hospital was entitled to 2018: JCI Patient Blood Management Certification.

Successful consequences obtained in the first step motivated the dissemination of the project in all

Table 3. University Hospital of Zurich-Patient blood management program organization

- Nominating a patient blood manager to educate representatives of surgical disciplines and making them adopt patient blood management over time
- Creating a commission for the responsible use of blood products (NOT traditional hemovigilance) as mandated by the Board of Directors via Medical Director and executed by both chairmen of Anesthesiology and Hematology
- Developing hospital-wide transfusion and coagulation management guidelines (for some "special" patients modifications are possible but should be strictly evidence-based)
- Establishing an intelligent blood ordering system
- Developing a monitoring and feedback system to collect data and assure the success of the program
- Developing an information technology program for early testing of focus patients (red blood cell transfusion rate ≥10% or expected blood loss ≥500 mL) for anemia and iron deficiency
- Giving early treatment aiming at a hemoglobin ≥130 g/L and no iron deficiency (ferritin ≥100 ng/mL and transferrin saturation [TSAT] ≥20%)

Table 4. 2016 data of Ankara Numune Training and Research Hospital

Ankara Numune Training and Research Hospital	
Total number of beds	1,140
Annual number of outpatient visits	1,768,649
Annual number of operations	55,469
Annual number of blood use	34,881 U
Cardiovascular Surgery Clinic	
Annual number of outpatient visits	34,445
Annual number of operations	1,318
Annual number of blood use (All operations by the department of cardiovascular surgery including emergency)	2,829 U • Whole blood 140 U • Erythrocyte suspension 855 U • Fresh frozen plasma 1667 U • Platelets 167 U

surgical clinics. Objectives of the program included determining the current situation, determining the problems in blood use, constituting a team of surgical branches, and holding meetings to form a strategic plan with the purpose of reducing blood use in the hospital by 50% in the 2018 to 2021 period. Approximately 35,000 units of total blood and blood products were utilized for about 55,000 operations at Numune Hospital in 2017. Figure 2 illustrates the distribution in some prominent branches.

The in-depth investigation highlighted the wastage of many of the unused blood products, which incurred a high cost equivalent to 16 triple coronary artery bypass surgeries (Table 5). As depicted in Table 6, the reasons for the destruction of blood and blood products were quite striking.

In 2018, hospital-wide blood and blood product usage dropped to 29,500 units, approximately. Therefore, a reduction in blood and blood product usage by 3% could be achieved in one year by conducting multidisciplinary scientific meetings and initiatives in surgical clinics of Numune Training and Research Hospital (Figure 3).

The data obtained from the Numune Hospital were published in various journals and presented at international congresses.[18-22] Subsequently, international training programs were launched in Turkey. The EuroAsia Heart Foundation decided to organize PBM Schools in Turkey, and the first meeting entitled Interdisciplinary Meeting on Bleeding Management in (Cardiac) Surgery and Obstetrics was held with 55 participants from 11 countries in Izmir in April 2019.

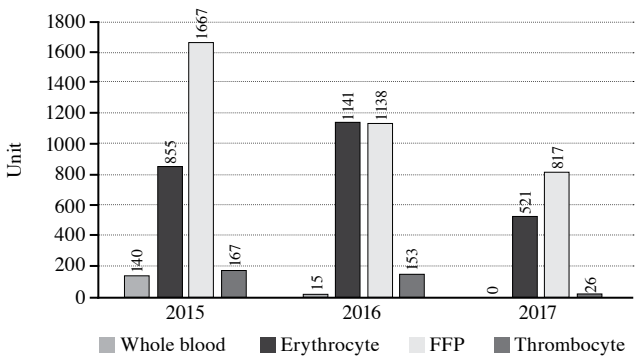

Figure 1. Ankara Numune Training and Research Hospital-the usage of blood and blood products in the cardiovascular surgery clinic by years (2015-2017 data).
FFP: Fresh frozen plasma.

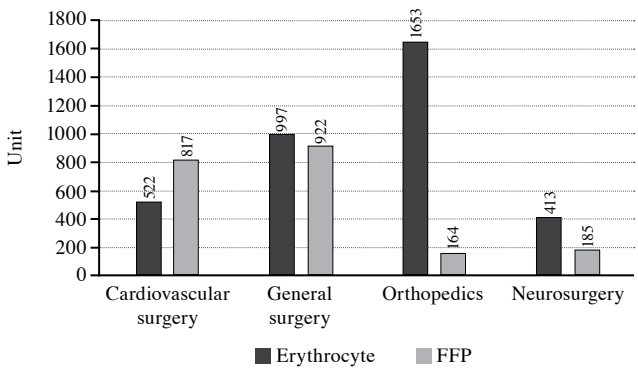

Figure 2. Ankara Numune Training and Research Hospital-the usage of blood products by branches (2017 data).
FFP: Fresh frozen plasma.

Table 5. Ankara Numune Training and Research Hospital - Used and destroyed blood products

	2016		2017 (January-September)	
	Used (U)	Destroyed (U)	Used (U)	Destroyed (U)
Erythrocyte suspension	13,805	329	9,527	188
	Random		Random	
Platelet suspension	2,476	89	_	_
	Pooled platelet (4 U)		Pooled platelet (4 U)	
	1,931	43	1,720	59
Fresh frozen plasma	12,964	330	7,768	192
Apheresis platelet suspension	816	21	316	7
Whole blood	17	2	_	_
Cryoprecipitate	235	_	425	5

U: Unit.

Consensus Meeting on PBM

The second stage of Numune Hospital's PBM program was decided to be continued in a larger scale hospital, which was established by the transportation of Ankara's largest state hospitals and put into service in December 2018. The city hospital comprises of 3,804 hospital beds, 735 outpatient clinics, and 128 operating theaters. The PBM has become one of the most important targets in the city hospital. The main objective of PBM implementation is to portray a good example for other hospitals in Turkey. The data gathered from the City Hospital on blood product usage and destruction are detailed in Tables 7 and 8.

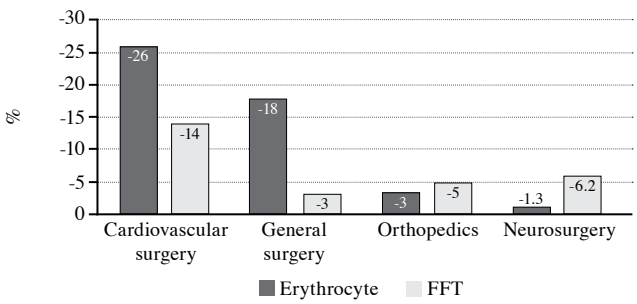

Figure 3. Ankara Numune Training and Research Hospital-reduction in blood products usage in one year (2018 data).
FFP: Fresh frozen plasma.

A strong organization, coupled with a multidisciplinary approach, is a prerequisite to cope with similar challenges during the implementation of PBM program in City Hospital.

Aiming at kick-off building a multidisciplinary PBM program in this extremely large hospital setting, a consensus meeting was organized to provide a platform where all components may come together to fix problems, discuss, and propose solutions. Over 150 participants in the meeting included members from the departments of anesthesiology, surgery, transplantation, ICU, perfusion, blood bank, nursing, pharmacy, and Ministry of Health. Professor Donat Spahn from the University Hospital of Zurich, being

Table 6. Ankara Numune Training and Research Hospital-Reasons for the destruction of blood products

Erythrocyte suspension (storage time: 42 days)	Platelet suspension (storage time: 5 days)	FFP (storage time: 2 years)	Apheresis platelet suspension (storage time: 5 days)
Passing the expiration date 94.15%	Passing the expiration date 100%	Returning after thawing 32.29%	Passing the expiration date 100%
Late returning from the services 5.85%		Product bag burst 67.71%	

FFP: Fresh frozen plasma.

Table 7. Ankara City Hospital Transfusion Center-used and destroyed blood products (February 2019-July 2019)

	Used (%)		Destroyed (%)		*Total*
	n	%	n	%	n
Erythrocyte suspension	12,847	96	467	4	13,314
Fresh frozen plasma	8,517	95	413	5	8,930
Pooled platelet suspension	1,532	89	184	11	1,716
Apheresis platelet suspension	49	84	9	16	58
Cryoprecipitate	1,158	94	71	6	1,229
Total	24,103	95	1,144	5	25,247

Table 8. Ankara City Hospital Transfusion Center-reasons for the destruction of blood products (February 2019-July 2019)

	Storage condition		Expiration date		Perforated bag		*Total*
	n	%	n	%	n	%	n
Erythrocyte suspension	127	27	333	71	7	2	467
Fresh frozen plasma	249	60	-	-	164	40	413
Pooled platelet suspension	4	2	178	97	2	1	184
Apheresis platelet suspension	-	-	9	100	-	-	9
Cryoprecipitate	62	87	2	3	7	10	71
Total	442	37	522	47	180	16	1144

1) Anesthesiology and Reanimation

Problems	**Solutions**
Inadequate diagnosis and treatment of preoperative anemia	Preoperative diagnosis and treatment of anemia, stabilization of comorbidities, physical optimization, deferring the operation if necessary, determining the patient's bleeding risk, and scheduling surgery accordingly[23]
Inappropriate, irrational, traditional blood and blood product transfusion	Management of anesthesia according to patient blood management, usage of tranexamic acid, retrograde autologous priming and autologous donation in the pump, providing qualified surgery and meticulous hemostasis, prevention of hypothermia after cardiopulmonary bypass, and optimization of cardiopulmonary functions[24]
Insufficient information in indications for the use of cryoprecipitate, fibrinogen concentrate, antifibrinolytic, and prothrombin complex concentrate	Ensuring the accuracy of the records of transfused patients by eradicating inappropriate blood stores
Inappropriate storage of blood in the clinics	Establishment of a local blood center unit in the common aisle of operating theaters and elimination of problems related to transport distances and staff securing the cold chain of blood products
Lack of well-defined protocols for various critical clinical situations (i.e., massive transfusion protocol, critical cardiac/pulmonary/renal disease protocols, critical transfusion thresholds, and reversal protocols in antiplatelet/anticoagulant use)	Multidisciplinary preparation of required protocols in accordance with the patient profile and defining the transfusion practices clearly and precisely in the hospital protocol

one of the leaders in the implementation of the PBM program, was invited and acted as a consultant.

In this multidisciplinary meeting, international and domestic experiences were shared, the importance of coordination and execution of different pillars in PBM was discussed, and the problems of the blood transfusion system were also explored with a proposal for solutions. Based on these data, it was aimed to develop a standard protocol for PBM which could be used as a guide by similar large-volume tertiary hospitals.[23,24]

There is not any purpose of comparison of any previous data with each other and/or with current situation. The geographic and background conditions of each instant are completely different. The main idea is to present different PBM protocols in various hospital settings.

Synopsis of Problems/Solutions

The following problems and proposals for the solutions were documented, discussed with managers, and a final consensus report was submitted for the hospital directorate.

2) Blood Transfusion Center

Problems	Solutions
New installation of the system/integration, automation problems	Training should continue uninterruptedly (nurse, physician, staff)
Distance between units	Rapid and safe transportation should be provided
Inexperienced allied health personnel	The opinions of experienced individuals working in the field should be acknowledged
Habitual malpractice	Blood and blood products must be preserved to the maximum extent, and their destruction should be strictly prohibited, except for medical reasons

3) Nursing Services

Problems	Solutions
Determination of blood type and cross-match (differently written blood type on the file and system, reaffirmation of blood types many times, sometimes labeling errors)	Use of blood barcode readers in clinics and an identity-check to be used for labeling the blood sample tube before leaving the bedside
Calling the blood center from the clinic to verify if the blood for cross-match has reached (waiting time on the phone, calling the blood center many times to check the cross-match)	Establishing an electronic blood monitoring system
Differences in the time of receiving the blood transfusion consent form	Ensuring standardization in filling the patient information section of the transfusion tracking form
Mode of transportation used to deliver the blood to the clinic	Rapid and safe transportation should be provided
Delivery of non-irradiated blood although irradiated blood was requested and return of blood for processing	Estimating compliance with hospital protocols/clinical guidelines in practice
Lack of pediatric blood bag	Should certainly be available
Different applications for transfusion tracking form according to the clinics (sometimes writing patient information manually, sometimes sticking barcode, sometimes second copy labeling error)	Use of simulation in blood transfusion training to ensure patient safety
No protocols of transfusion for emergency and extracorporeal membrane oxygenation patients	Proper education and training regarding clinical guidelines provided to the health professionals on blood product transfusion and patient blood management

1) Anesthesiology and Reanimation

2) Blood Transfusion Center

3) Nursing Services

The blood transfusion procedures of our hospital are prepared following the national guidelines, National Blood and Blood Components Preparation, Use and Quality Assurance Guideline-2016,[25] and National Hemovigilance Guideline-2016.[26] According to these blood transfusion procedures, monitoring, educating, reporting, analysis, and documentation of blood transfusion applications are the responsibilities of our hemovigilance nurses.

4) Intensive care unit

5) Transplantation Services

6) Perfusion Services

Conclusion

The liberal RBC transfusion approaches can effectively achieve restoration of hemoglobin concentrations toward non-anemic values; however,

4) Intensive care unit

Problems	Solutions
Varying indications of transfusion in different intensive care unit (ICU) units	Active use of guidelines in clinical practice
Problems in accessing the blood product (particularly in emergencies) and transportation problems	Rapid and safe transportation
Blood product storage problems	Establishment of a local blood center unit in the common aisle of ICUs and elimination of problems related to transport distances and staff
Lack of interdisciplinary communication	Establishing a transfusion strategy in compliance with the hospital conditions and employee profile
Transfusion-related complications	Collecting statistical data and feedbacks (i.e., percentages blood product use, mortality, morbidity, length of stay in the hospital, and ICU, mean pretransfusion values, and costs)

5) Transplantation Services

Problems	Solutions
Late arrival of the blood products is the major problem.	Rapid and safe delivery
Problems with the management of the hospital	Appointing the hospital as a blood donation center, providing viscoelastic testing and new oral anticoagulant antidotes to the hospital
Authority issues related to allied health personnel	Defining duties of the personnel in a guideline
Different indications with different physicians	Establishing a common diagnosis and treatment approach for the management of anemia

6) Perfusion Services

Problems	Solutions
Varying perfusion protocols for different surgeons	Developing an institutional culture and determining common protocols
Different approaches in different disciplines in the operating room	Being in contact with surgeons, anesthesiologists, and perfusionists avoiding interference of each other's applications
No experience in novel extracorporeal technologies for avoiding perioperative bleeding in cardiovascular surgery	Ensuring the use of autotransfusion devices, mini-circuits, vacuum-assisted venous drainage, retrograde autologous priming and centrifugal pumps in every appropriate case

transfusion of stored allogeneic RBCs does not correct the primary metabolic deficiencies associated with anemia, nor does it restore iron homeostasis. On the other hand, it has become a common practice to transfuse stable patients with low hemoglobin without symptoms of anemia.[27]

Despite the demonstrated benefits of PBM, several challenges limit the application of PBM guidelines into clinical practice worldwide, particularly due to the lack of knowledge, lack of interdisciplinary commitment, lack of resources, and general concerns. It should enable PBM's patient-centered approach to be delivered in a way that is also hospital centered and, therefore, compatible with each institution. The initial success achieved from the institution should impart further motivation and activities in the field of PBM.[28,29]

Pillars need to be adapted with respect to characteristics of the region and legislations available. For instance, there are specific reimbursement policies for IV iron therapy in Turkey. Also, limitations of the use of EPO and vitamin B12/folic acid by nephrologists may become a burden for cardiac surgeons to implement perioperative anemia correction. Successful PBM implementation involves structural changes, logistic reorganizations and leadership with psychological skills, a monitoring, and feedback program, and persistence. An individualized program must be established by the hospitals with the consensus of participants.

The Ankara City Hospital is the largest hospital in Turkey. Current practice with the use of more than 60,000 units of blood and blood products in one year necessitates the need for a PBM program.

We believe that this consensus report would accelerate the cooperation within disciplines and provoke more optimal results in the short-term. Furthermore, it is valuable as it represents a guide for similar large-volume hospital settings.

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